

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 August 2005 (11.08.2005)

PCT

(10) International Publication Number
WO 2005/072084 A2

(51) International Patent Classification: Not classified

(21) International Application Number:
PCT/US2004/039318

(22) International Filing Date:
23 November 2004 (23.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/721,034 24 November 2003 (24.11.2003) US

(71) Applicant (for all designated States except US):
ETHICON ENDO-SURGERY, INC. [US/US]; 4545
Creek Road, Cincinnati, OH 45242 (US).

(71) Applicants and

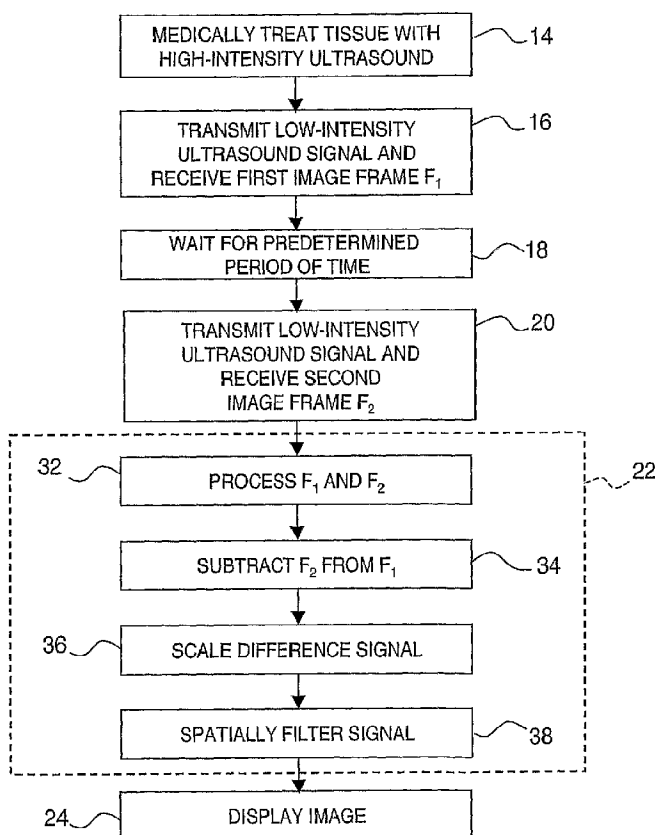
(72) Inventors: **MAST, T., Douglas** [US/US]; 3907 Lands-
downe Avenue, Cincinnati, OH 45236 (US). **MAKIN, In-
der, Raj, S.** [US/US]; 11388 Donwiddle Drive, Loveland,
OH 45140 (US). **BARTHE, Peter, G.** [US/US]; 4818-1
E.Hazel Drive, Phoenix, AZ 85044 (US). **FAIDI, Waseem**
[US/JO]; 702 Solomon Avenue, Clifton Park, NY 12065
(US). **SLAYTON, Michael, H.** [US/US]; 1323 E.Whalers
Way, Tempe, AZ 85283-2149 (US).

(74) Agents: **JOHNSON, Phillip, S.** et al.; Johnson & Johnson,
1 Johnson & Johnson Plaza, New Brunswick, NJ 08933
(US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,

[Continued on next page]

(54) Title: METHOD FOR MONITORING OF MEDICAL TREATMENT USING PULSE-ECHO ULTRASOUND



(57) Abstract: A method for ultrasound imaging of anatomical tissue. A first signal is received from a first imaging ultrasound wave which has been reflected from a location in the anatomical tissue during a first time period. A second signal is received from a second imaging ultrasound wave which has been reflected from the location in the anatomical tissue during a later second time period, following a discrete medical treatment. The second signal is subtracted from the first signal to form a difference signal. The difference signal may be scaled, spatially filtered, then used to generate an indication, the indication showing the effect of the medical treatment in the location in the anatomical tissue.



MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE,

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

- 1 -

**METHOD FOR MONITORING OF MEDICAL TREATMENT
USING PULSE-ECHO ULTRASOUND**

[0001] Field of the Invention

[0002] This is a continuation-in-part of Application No. 10/153,241, filed May 22, 2002, which claims priority to provisional application serial number 60/294,135 filed May 29, 2001. The present invention relates generally to ultrasound, and more particularly, to an ultrasound medical imaging method.

[0003] Background of the Invention

[0004] Ultrasound medical systems and methods include ultrasound imaging of anatomical tissue to identify tissue for medical treatment. Ultrasound may also be used to medically treat and destroy unwanted tissue by heating the tissue. Imaging is done using low-intensity ultrasound waves, while medical treatment is performed with high-intensity ultrasound waves. High-intensity ultrasound waves, when focused at a focal zone a distance away from the ultrasound source, will substantially medically affect tissue in the focal zone. However, the high-intensity ultrasound will not substantially affect patient tissue outside the focal zone, such as tissue located between the ultrasound source and the focal zone. Other treatment regimes of interest include unfocused high-intensity ultrasound, wherein the ultrasound energy is distributed over a relatively broad region of tissue rather than being generally concentrated within a focal zone.

[0005] Ultrasound waves may be emitted and received by a transducer assembly. The transducer assembly may include a single element, or an array of elements acting together, to image the anatomical tissue and to ultrasonically ablate identified tissue. Transducer elements may employ a concave shape or an acoustic lens to focus ultrasound energy. Transducer arrays may include planar, concave or convex elements to focus or otherwise direct

- 2 -

ultrasound energy. Further, such array elements may be electronically or mechanically controlled to steer and focus the ultrasound waves emitted by the array to a focal zone to provide three-dimensional medical ultrasound treatment of anatomical tissue. In some treatments the transducer is placed on the surface of the tissue for imaging and/or treatment of areas within the tissue. In other treatments the transducer is surrounded with a balloon which is expanded to contact the surface of the tissue by filling the balloon with a fluid such as a saline solution to provide acoustic coupling between the transducer and the tissue.

[0006] Examples of ultrasound medical systems and methods include: deploying an end effector having an ultrasound transducer outside the body to break up kidney stones inside the body; endoscopically inserting an end effector having an ultrasound transducer into the rectum to medically destroy prostate cancer; laparoscopically inserting an end effector having an ultrasound transducer into the abdominal cavity to destroy a cancerous liver tumor; intravenously inserting a catheter end effector having an ultrasound transducer into a vein in the arm and moving the catheter to the heart to medically destroy diseased heart tissue; and interstitially inserting a needle end effector having an ultrasound transducer into the tongue to medically destroy tissue to reduce tongue volume as a treatment for snoring. Methods for guiding an end effector to the target tissue include x-rays, Magnetic Resonance Images ("MRI") and images produced using the ultrasound transducer itself.

[0007] Low-intensity ultrasound energy may be applied to unexposed anatomical tissue for the purpose of examining the tissue. Ultrasound pulses are emitted, and returning echoes are measured to determine the characteristics of the unexposed tissue. Variations in tissue structure and tissue boundaries have varying acoustic impedances, resulting in variations in the strength of ultrasound echoes. A common ultrasound imaging technique is known in the art as "B-Mode" wherein either a single ultrasound transducer is articulated or an array of ultrasound transducers is moved or electronically scanned to generate a two-dimensional image of an area of tissue. The generated image is comprised of a plurality

- 3 -

of pixels, each pixel corresponding to a portion of the tissue area being examined. The varying strength of the echoes is preferably translated to a proportional pixel brightness. A cathode ray tube or liquid crystal display can be used to display a two-dimensional pixellated image of the tissue area being examined. varying strength of the echoes is preferably translated to a proportional pixel brightness. A cathode ray tube or liquid crystal display can be used to display a two-dimensional pixellated image of the tissue area being examined.

[0008] When high-intensity ultrasound energy is applied to anatomical tissue, significant beneficial physiological effects may be produced in the tissue. For example, undesired anatomical tissue may be ablated by heating the tissue with high-intensity ultrasound energy. By focusing the ultrasound energy at one or more specific focusing zones within the tissue, thermal effects can be confined to a defined region that may be remote from the ultrasound transducer. The use of high-intensity focused ultrasound to ablate tissue presents many advantages, including: reduced patient trauma and pain; potentially reduced patient recovery time; elimination of the need for some surgical incisions and stitches; reduced or obviated need for general anesthesia; reduced exposure of non-targeted internal tissue; reduced risk of infection and other complications; avoidance of damage to non-targeted tissue; avoidance of harmful cumulative effects from the ultrasound energy on the surrounding non-target tissue; reduced treatment costs; minimal blood loss; and the ability for ultrasound treatments to be performed at non-hospital sites and/or on an out-patient basis.

[0009] Ultrasound treatment of anatomical tissue may involve the alternating use of both low-intensity imaging ultrasound and high-intensity treatment ultrasound. During such treatment, imaging is first performed to identify and locate the tissue to be treated. The identified tissue is then medically treated with high-intensity ultrasound energy for the purpose of ablating the tissue. After a period of exposure to high-intensity ultrasound, a subsequent image of the tissue is generated using low-intensity ultrasound energy to determine the results of the ultrasound treatment and provide visual guidance to the user

- 4 -

to aid in subsequent treatments. This process of applying low-energy ultrasound to assist in guiding the position and focal point of the transducer, followed by high-energy ultrasound to ablate the undesired anatomical tissue, may continue until the undesired tissue has been completely ablated.

- [0010]** Although this conventional B-Mode ultrasound imaging provides an effective means for imaging tissue that is in a static state, imaging of the tissue becomes more problematic when used in conjunction with thermal high-intensity ultrasound treatment. As the tissue is ablated during treatment, the heating effects of ultrasound upon the tissue often result in qualitative changes in echo strength, causing brightness variations in the pixel display that do not consistently correspond spatially to the tissue being treated. These brightness variations result in an image display that does not represent the actual shape and size of the region of tissue that is being thermally modified by the treatment, introducing some visual ambiguity to the image.
- [0011]** Several methods are known for monitoring thermal ablation using B-Mode ultrasound imaging. Most of these are based on changes in the energy of ultrasound echoes, and include simple B-Mode displays of echo amplitude, estimates of tissue attenuation from analysis of distal shadowing, and quantification of changes in echo energy. Each of these methods have significant shortcomings because the tissue being treated can appear hyperechoic for reasons other than thermal ablation and because image changes must be qualitatively perceived by the user.
- [0012]** The most successful known methods for monitoring thermal ablation using ultrasound are based on analysis of changes in echo energy rather than a direct analysis of the echo energy. Automatic and quantitative displays of changes in echo energy or tissue attenuation are possible and can help users isolate thermally-induced changes from pre-existing echo characteristics. However, since such methods require integration of echoes over substantial regions of an image scan or "frame," the resulting images are very limited in spatial resolution. Although energy increases (and therefore B-Mode

- 5 -

brightness increases) correspond roughly to lesion (i.e., the thermally treated tissue) position, typically the shape and size of the mapped energy increases do not always spatially correspond to actual lesions, and sometimes are either absent or otherwise unapparent.

[0013] There is a need for an improved method of ultrasound imaging that can be utilized in conjunction with therapeutic ultrasound treatment that monitors the thermal effects of the treatment on targeted tissue with greater accuracy and resolution.

[0014] **Summary of the Invention**

[0015] The present invention overcomes the limitations of the known art by mapping differences between a first and second echo signal, each signal being obtained at different instants of time. The first and second signals are typically separated by a small time interval. The first and second signals are processed, then a measure of the amplitude of the differences between the first and second signals is made (as contrasted with a measure of the differences in signal amplitude). This difference signal is then spatially filtered and scaled to quantify echo changes associated with changes in tissue state. Difference signals may be summed over multiple time periods to obtain a cumulative map of the changes in the tissue. The resulting signals may be used to generate an ultrasound image that is more representative of the tissue as treatment progresses, providing additional information about where thermal effects are occurring. This allows for verification of successful treatment and modification of unsuccessful treatment. Known ultrasound imaging and treatment transducers may be used, providing users with increased accuracy without a need for special end effectors.

[0016] **Brief Description of the Drawings**

[0017] Further features of the present invention will become apparent to those skilled in the art to which the present invention relates from reading the following specification with reference to the accompanying drawings, in which:

- 6 -

- [0018] Fig. 1 is a flow diagram providing an overview of an ultrasound treatment method according to an embodiment of the present invention;
- [0019] Fig. 2 illustrates the relative amplitude and timing of ultrasound image frames and ultrasound treatments of the method of Fig. 1;
- [0020] Fig. 3 is a flow diagram of a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to an embodiment of the present invention;
- [0021] Fig. 4 is a view of a first ultrasound signal on a time scale;
- [0022] Fig. 5 is a view of a second ultrasound signal on a time scale;
- [0023] Fig. 6 is a composite view of the signals of Fig. 4 and Fig. 5;
- [0024] Fig. 7 is a view showing the difference signal computed from Fig. 4 and Fig. 5;
- [0025] Fig. 8 is a view showing the absolute value of the difference signal of Fig. 7;
- [0026] Fig. 9 is a view of the signal of Fig. 8 after filtering;
- [0027] Fig. 10 is a flow diagram depicting a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to an alternate embodiment of the present invention;
- [0028] Fig. 11 illustrates the relative amplitude and timing of ultrasound image frames, image frame sets and ultrasound treatments of the method of Fig. 10;
- [0029] Fig. 12 depicts a flow diagram of a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to another alternate embodiment of the present invention;
- [0030] Fig. 13 shows the relative amplitude and timing of ultrasound image frame sets, difference signals and ultrasound treatments of the method of Fig. 12;

- 7 -

[0031] Fig. 14 is a flow diagram of a method for monitoring medical treatment of anatomical tissue using pulse-echo ultrasound according to yet another alternate embodiment of the present invention; and

[0032] Fig. 15 shows the relative amplitude and timing of ultrasound image frames and ultrasound treatments of the method of Fig. 14.

[0033] **Detailed Description**

[0034] An overview of an ultrasound treatment method 10 according to an embodiment of the present invention is shown in Fig. 1. The method begins at step 12 by positioning proximate the targeted anatomical tissue to be medically treated a transducer capable of transmitting and receiving ultrasound signals. Once the transducer is in position, treatment begins at step 14 by emitting a high-intensity ultrasound signal from the transducer. The high-intensity ultrasound signal medically treats the targeted tissue, such as (but not limited to) heating the tissue to ablate the material. At step 16 a low-intensity ultrasound signal, such as a B-Mode signal, is emitted from the transducer and the reflected signals are received to form a first image frame F_1 . It is understood that the terminology "image" includes, without limitation, creating an image in a visual form and displayed, for example, on a monitor, screen or display, and creating an image in electronic form which, for example, can be used by a computer without first being displayed in visual form. After the first image frame F_1 is received at step 16, a predetermined waiting period is executed at step 18 before proceeding further. It is to be understood that the predetermined waiting period may vary in value from zero seconds upwardly to a maximum of several seconds, but preferably is in the range of milliseconds. After the predetermined wait period has been completed, a low intensity ultrasound signal is again emitted from the transducer and a second image frame F_2 is received at step 20. At step 22 a difference signal is derived from the image frames F_1 and F_2 , as will be discussed in greater detail below. The difference signal of step 22 is displayed as an image at step 24 to obtain a visual indication of the tissue change as a

- 8 -

result of the medical treatment of step 14. It should be noted that the visual indication of the tissue change provided by the present invention differs from the post-treatment image of the prior art in that the present invention provides an image showing echo differences in contrast to echos from the target tissue. The image of echo differences can indicate whether treatment is complete. If treatment is complete at step 26 (for example, the targeted tissue has been fully ablated), the method is ended at step 28. However, if the tissue requires additional treatment, the transducer may be re-positioned at step 30. The method then returns to step 14 to continue medical treatment of the targeted tissue.

[0035] Referring additionally to Fig. 2, the method of Fig. 1 is illustrated in relation to a time scale t . The targeted tissue is medically treated with a relatively high-intensity ultrasound signal as at step 14. Then, at step 16 a relatively low-intensity B-Mode image scan frame F_1 is received. After a predetermined off-time, as at step 18, a second image frame F_2 is received, as at step 20. The image frames F_1 and F_2 each contain a signal representing the same portion of the target tissue. For each image frame, a number of A-lines of raw echo signal data are received, the number of each line corresponding to azimuthal position and the signal time corresponding to depth.

[0036] Referring now to Fig. 3 in combination with Figs. 1 and 2, a method for monitoring medical treatment of anatomical tissue including, but not limited to, thermal ablation according to an embodiment of the present invention is depicted. An ultrasound transducer is positioned proximate the targeted anatomical tissue. The tissue may then be medically treated such as by ablation using high-intensity ultrasound waves for a period of time as at step 14. At step 16 a first image frame F_1 (such as is illustrated in Fig. 4) is received. The image frame may optionally be stored electronically, such as in a computer, magnetic media and solid-state memory. A second image frame F_2 , separated from F_1 by a fixed time interval of step 18, is received at step 20. An example image frame F_2 is illustrated in Fig. 5. A difference signal is then derived at step 22 by means of steps 32-38. The raw echo signals of frames F_1 and F_2 may be processed at step 32, such as to obtain complex analytic signals by means of a Hilbert transformation. \hat{A}

- 9 -

difference signal may then be derived by subtracting the signal of image frame F_2 from the signal of F_1 at step 34. The difference signal of step 34 may take into account both phase and amplitude differences between F_1 and F_2 , computing the amplitude of the signal differences (as opposed to differences in signal amplitude) of F_1 and F_2 . A composite illustration of image frames F_1 and F_2 is shown in Fig. 6, while the derived difference signal is depicted in Fig. 7. At step 36 the difference signal may be scaled to a convenient value, such as the mean squared value of the difference signal, the mean squared value of one of the original echo signals, or a mathematical constant. As an example, a signal representing the scaled absolute value of the difference signal of Fig. 7 is shown in Fig. 8. Other functions of the difference signal, such as its squared absolute value or logarithm, may similarly be employed. Still other scaling algorithms may use the amplitude and/or phase of the first and second signals to enhance differences between the first and second signals. Details of such algorithms are left to the skilled artisan. At step 38 the difference signal is spatially filtered, as depicted in Fig. 9, to smooth small-scale random variations. Spatial filtering of the scaled difference signal is represented by Equation 1.

$$[0037] \quad \Psi(x, z) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} w(x-x_0, z-z_0) \left| p_0(x_0, z_0) - p_1(x_0, z_0) \right|^2 dx_0 dz_0$$

[0038] **Equation 1**

[0039] In Equation 1 Ψ is a spatial difference map (image) of the scaled and filtered difference signal. The filtering may be performed by convolution of the scaled difference signal with a two-dimensional window w . This convolution may be efficiently performed through the use of two-dimensional Fast Fourier Transform ("FFT") operations.

[0040] The difference signal may be normalized to have a maximum value of 1. This approach would result in a spatial map of the echo decorrelation, similar to measures of turbulence in color Doppler imaging systems. However, instead of examining echo decorrelation (a normalized measure of echo differences), a non-normalized map is considered preferable

- 10 -

for the present invention because the echo difference is then enhanced in regions of greater echogenicity. Since hyperechoicity is one correlate to tissue ablation, this feature increases the specificity of the method for monitoring thermal ablative medical treatment by providing an image with greater detail.

[0041] The spatially filtered signal of Fig. 9 is then displayed as an image at step 24 (see Fig. 3), in any manner previously discussed.

[0042] In a second embodiment of the present invention, ultrasound images may be generated as depicted in Figs 10 and 11. At step 40 the tissue is medically treated with high-intensity ultrasound waves. At step 42 a succession of image frames, depicted as $F_1, F_2, \dots F_n$, are received. The image frames $F_1, F_2, \dots F_n$ each contain a signal representing the same portion of the target tissue. At step 44 the image frames $F_1, F_2, \dots F_n$ are mathematically grouped, such as by summing or averaging, to form a first image frame set labeled FS_1 , as shown in Fig. 11. After waiting a predetermined amount of time, as at step 46, a second set of image frames $F_1, F_2, \dots F_n$ are received at step 48. At step 50 the second set of image frames $F_1, F_2, \dots F_n$ are mathematically grouped, such as by summing or averaging, to form a second image frame set FS_2 as shown in Fig. 11. The raw echo signals of image frame sets FS_1 and FS_2 may be processed at step 52, such as to derive complex analytic signals by means of a Hilbert transformation. The signal of image frame set FS_2 is then subtracted from the signal of image frame set FS_1 at step 54 to derive a difference signal. The difference signal may take into account both phase and amplitude differences between FS_1 and FS_2 , computing the amplitude of the signal differences (as opposed to differences in signal amplitude) of FS_1 and FS_2 . At step 56 the difference signal may be scaled to a convenient value using any scaling methods and algorithms, previously described or otherwise. At step 58 the difference signal is spatially filtered to smooth small-scale random variations before being displayed as an image at step 59. This embodiment of the present invention may provide a more robust map of the backscatter changes by reducing the influence of random signal variations

- 11 -

caused by rapid transient effects such as violent bubble activity produced during tissue ablation.

[0043] In a third embodiment of the present invention, smoothing of the image signal may alternatively be accomplished by using a plurality of image frames, as illustrated in Figs. 12 and 13. The tissue is medically treated at step 60, then a set of image frames $F_1, F_2, \dots F_n$ are received at step 62. A plurality of difference signals $D_1, D_2, \dots D_n$ are computed at step 64. It should be noted that the difference signals may be computed using various arrangements of pairs of image frames. For example, difference signal D_1 may be formed by subtracting F_2 from F_1 ; likewise, D_2 may be formed by subtracting F_3 from F_2 , as shown in Fig. 13. Other arrangements of image frame pairs may also be used, including (but not limited to) odd-numbered image frames (i.e., subtracting F_3 from F_1 , etc.) and even-numbered image frames (i.e., subtracting F_4 from F_2 , etc.). The pairings may be interlaced (i.e., subtracting F_2 from F_1 , subtracting F_3 from F_2 , etc.) or sequential (i.e., subtracting F_2 from F_1 , F_4 from F_3 , etc.). An indication or image may be displayed at step 66, showing at least one of the difference signals $D_1, D_2, \dots D_n$. At step 68 the difference signals $D_1, D_2, \dots D_n$ may be further processed, such as by averaging, to reduce artifactual content. The averaged signal, denoted as \bar{D} , may also be displayed as an image, as at step 70. The averaged signals may themselves be cumulatively summed, as at step 72, to provide a view of the results of successive medical treatments 60. The summed averages may be displayed at step 74. If treatment is determined to be complete at step 76, the method is ended at step 78. However, if the tissue appears to require additional treatment, the transducer may be re-positioned at step 80. The method is then repeated beginning at step 60 to continue treatment of the targeted tissue.

[0044] A fourth embodiment of the present invention is shown in Figs. 14 and 15 wherein a difference signal is derived using imaging frames generated both before and after medical treatment. At step 82 the ultrasound transducer is positioned proximate the targeted tissue to be medically treated. At step 84 a pre-treatment image frame F_1 is generated from received ultrasound signals. Then, at step 86 the tissue is subject to a quantum of

- 12 -

medical treatment, such as by ablating the tissue. After a quantum of medical treatment is administered, a second image frame F_2 is generated at step 88. A difference signal is derived at step 90, using the data contained in image frames F_1 and F_2 in the same manner as previously described. An indication or image of the difference signal may be displayed at step 92. If treatment is determined to be complete at step 94, the method is ended at step 96. However, if the targeted tissue is determined to require additional treatment, the transducer may be re-positioned as necessary at step 98. The method is then repeated and a subsequent quantum of treatment is administered beginning at step 84.

[0045] An expected difficulty for the present invention is artifactual backscatter change due to tissue motion artifacts. This difficulty can be largely overcome by several features of the method. First, backscatter differences can be computed between image frames closely spaced in time. If the tissue moves only a small amount during the interval, motion artifacts are then small. Second, artifacts due to axial tissue motion can be removed effectively by phase compensation during signal processing. That is, before computation of the signal difference, one of the complex image frames is multiplied by a phase compensation function $e^{-i\theta}$, where θ is the low-pass filtered phase of the conjugate product of the two complex image frames. The resulting signal difference is then computed, for example, using Equation 2:

[0046]
$$\Psi = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} w(x, z) \left| p_0(x, z) - p_1(x, z) e^{-i\varphi_0 \delta} \right|^2 dx dz$$

[0047] Equation 2

[0048] which is an improved echo difference map with reduced tissue motion artifacts.

[0049] It is understood that one or more of the previously-described embodiments, expressions of embodiments, examples, methods, etc. can be combined with any one or more of the other previously-described embodiments, expressions of embodiments, examples,

- 13 -

methods, etc. For example, and without limitation, any of the ultrasound transducers may be used with other methods of medical treatment, such as producing images to aid in tissue ablation by means of Radio Frequency (RF) and laser energy, various non-ablative ultrasound medical treatments, and various ultrasound imaging applications.

[0050] The foregoing description of several expressions of embodiments and methods of the invention has been presented for purposes of illustration. It is not intended to be exhaustive or to limit the present invention to the precise forms and procedures disclosed, and obviously many modifications and variations are possible in light of the above teaching. It is intended that the scope the invention be defined by the claims appended hereto.

WHAT IS CLAIMED IS:

1. A method for ultrasound imaging of anatomical tissue, comprising the steps of:
 - a) receiving a first signal of a first imaging ultrasound wave which has been reflected from a location in the anatomical tissue during a first time period;
 - b) receiving a second signal of a second imaging ultrasound wave which has been reflected from the location in the anatomical tissue at a later second time period following a discrete medical treatment;
 - c) subtracting the second signal from the first signal to derive a difference signal;
 - d) generating an indication from the difference signal, the indication showing the effect of the discrete medical treatment in the location in the anatomical tissue.
2. The method of claim 1 wherein the first and second signals are received after the discrete medical treatment has been completed.
3. The method of claim 1 wherein the first signal is received before the discrete medical treatment, and the second signal is received after the discrete medical treatment has been completed.
4. The method of claim 1, further comprising the step of processing the first and second signals.
5. The method of claim 4, further comprising the step of multiplying at least one of the first and second signals by a phase compensation function to reduce motion artifacts.
6. The method of claim 1, further comprising the step of scaling the difference signal.
7. The method of claim 6 wherein the difference signal is scaled by squaring the amplitude of the difference signal.
8. The method of claim 1, further comprising the step of spatially filtering the difference signal.

- 15 -

9. The method of claim 1, wherein the medical treatment is ultrasound medical treatment.

10. The method of claim 1, also including the steps a) through d) for different locations to image the anatomical tissue, wherein the image includes medically-treated locations and medically-untreated locations of the anatomical tissue.

11. The method of claim 1, further comprising the step of combining the difference signal image with a second image of the location in the anatomical tissue.

12. The method of claim 11 wherein the second image is generated using a B-Mode ultrasound scan.

13. A method for ultrasound imaging of anatomical tissue, comprising the steps of:

a) receiving a first signal of a first imaging ultrasound wave which has been reflected from a location in the anatomical tissue during a first time period;

b) receiving a second signal of a second imaging ultrasound wave which has been reflected from the location in the anatomical tissue at a later second time period following a discrete medical treatment;

c) processing the first and second signals;

d) subtracting the second signal from the first signal to derive a difference signal;

e) scaling the difference signal;

f) spatially filtering the difference signal; and

g) generating an indication from the difference signal, the indication showing the effect of the discrete medical treatment in the location in the anatomical tissue.

14. The method of claim 13 wherein the first and second signals are received after the discrete medical treatment has been completed.

- 16 -

15. The method of claim 13 wherein the first signal is received before the discrete medical treatment and the second signal is received after the discrete medical treatment.

16. A method for ultrasound imaging of anatomical tissue, comprising the steps of:

- a) receiving a first set of image frames comprising a plurality of imaging ultrasound wave signals which have been reflected from a location in the anatomical tissue during a first period of time;
- b) receiving a second set of image frames comprising a plurality of imaging ultrasound wave signals which have been reflected from the location in the anatomical tissue during a later second period of time following a discrete medical treatment;
- c) subtracting the imaging ultrasound signals of the second set of image frames from the imaging ultrasound signals of the first set of image frames to derive a difference signal; and
- d) generating an indication from the difference signal, the indication showing the effect of the discrete medical treatment in the location in the anatomical tissue.

17. The method of claim 16 wherein the first and second sets of image frames are received after the discrete medical treatment has been completed.

18. The method of claim 16 wherein the first set of image frames is received before the discrete medical treatment, and the second set of image frames is received after the discrete medical treatment.

19. The method of claim 16, further comprising the step of processing the first and second sets of signals.

20. The method of claim 16, further comprising the step of scaling the difference signal.

21. The method of claim 20 wherein the difference signal is scaled by squaring the amplitude of the difference signal.

- 17 -

22. The method of claim 16, further comprising the step of spatially filtering the difference signal.

23. The method of claim 16, wherein the medical treatment is ultrasound medical treatment.

24. The method of claim 16, also including the steps a) through d) for different locations to image the anatomical tissue, wherein the image includes medically-treated locations and medically-untreated locations of the anatomical tissue.

25. A method for ultrasound imaging of anatomical tissue, comprising the steps of:

a) receiving a first set of image frames comprising a plurality of imaging ultrasound wave signals which have been reflected from a location in the anatomical tissue during a first period of time;

b) receiving a second set of image frames comprising a plurality of imaging ultrasound wave signals which have been reflected from the location in the anatomical tissue during a later second period of time following a discrete medical treatment;

c) processing the first and second sets of signals;

d) subtracting the imaging ultrasound signals of the second set of image frames from the ultrasound signals of the first set of image frames to derive a difference signal;

e) scaling the difference signal;

f) spatially filtering the difference signal; and

g) generating an indication from the difference signal, the indication showing the effect of the discrete medical treatment in the location in the anatomical tissue.

26. The method of claim 25 wherein the first and second sets of image frames are received after the discrete medical treatment has been completed.

- 18 -

27. The method of claim 25 wherein the first set of image frames is received before the discrete medical treatment, and the second set of image frames is received after the discrete medical treatment.

28. The method of claim 25 wherein the medical treatment is ultrasound medical treatment.

29. The method of claim 25, also including the steps a) through g) for different locations to image the anatomical tissue, wherein the image includes medically-treated locations and medically-untreated locations of the anatomical tissue.

30. A method for ultrasound imaging of anatomical tissue, comprising the steps of:

- a) providing a discrete medical treatment to the anatomical tissue;
- b) receiving a set of image frames comprising a plurality of imaging ultrasound wave signals which have been reflected from a location in the anatomical tissue;
- c) pairing together a plurality of image frames, each pair comprising a first image frame and a second image frame such that the second image frame has been reflected from a location in the anatomical tissue at a later time than the first image frame;
- d) subtracting the signals of the second image frame from the signals of the first image frame, for each pair of image frames in the image frame set, to derive a set of difference signals;
- e) using at least one difference signal to generate an indication showing the effect of the discrete medical treatment in the location in the anatomical tissue; and
- f) repeating steps a) through e) until medical treatment is completed.

31. The method of claim 30, further comprising the steps of:

- 19 -

- a) computing an average of the set of difference signals; and
- b) using the average of the set of difference signals to generate an indication showing the effect of the discrete medical treatment in the location in the anatomical tissue.

32. The method of claim 31, further comprising the steps of:

- a) cumulatively summing the averages of the set of difference signals; and
- b) using the cumulative sum of averages of the set of difference signals to generate an indication showing the effect of the discrete medical treatment in the location in the anatomical tissue.

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 1 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

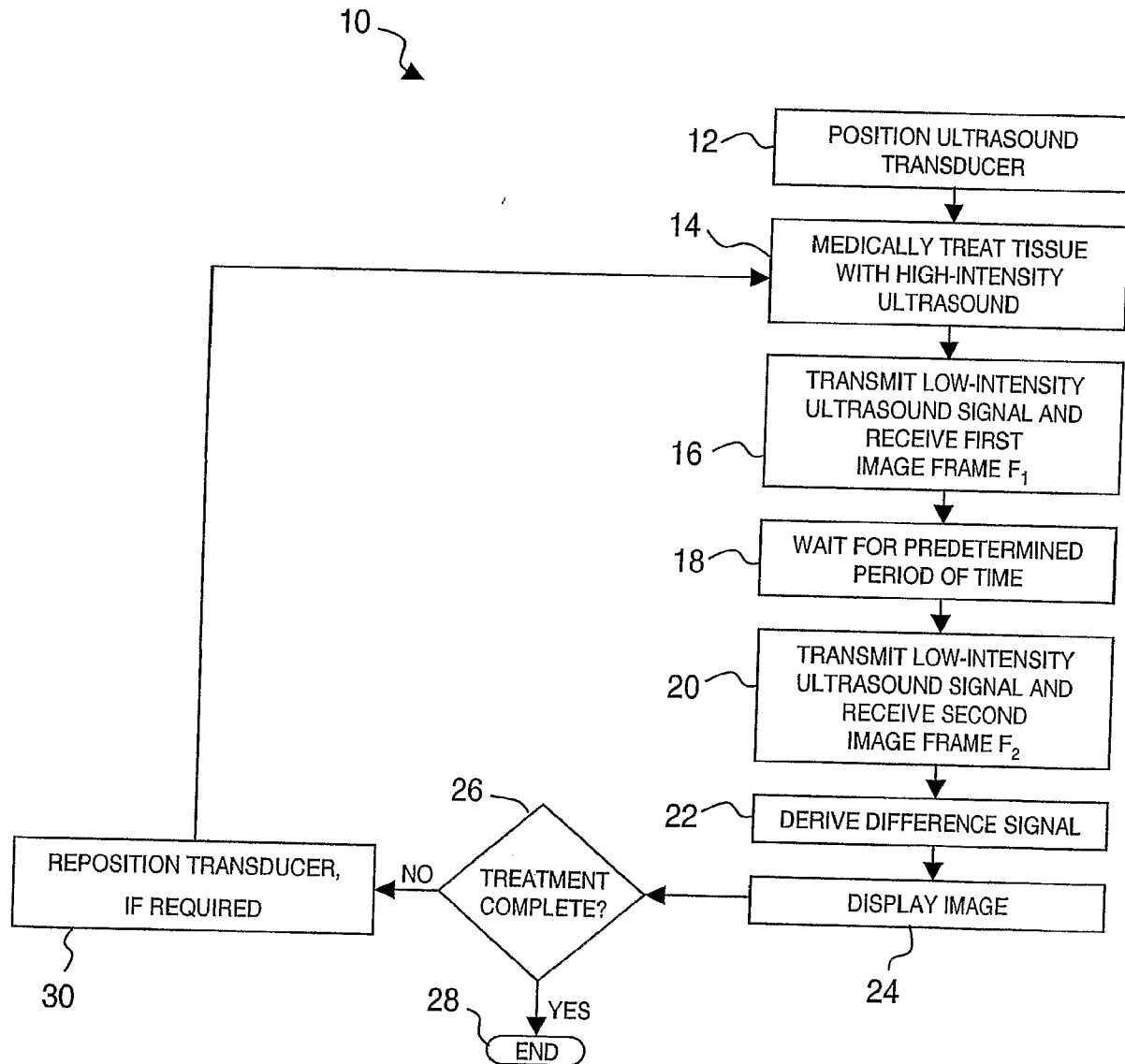


Fig. 1

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 2 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

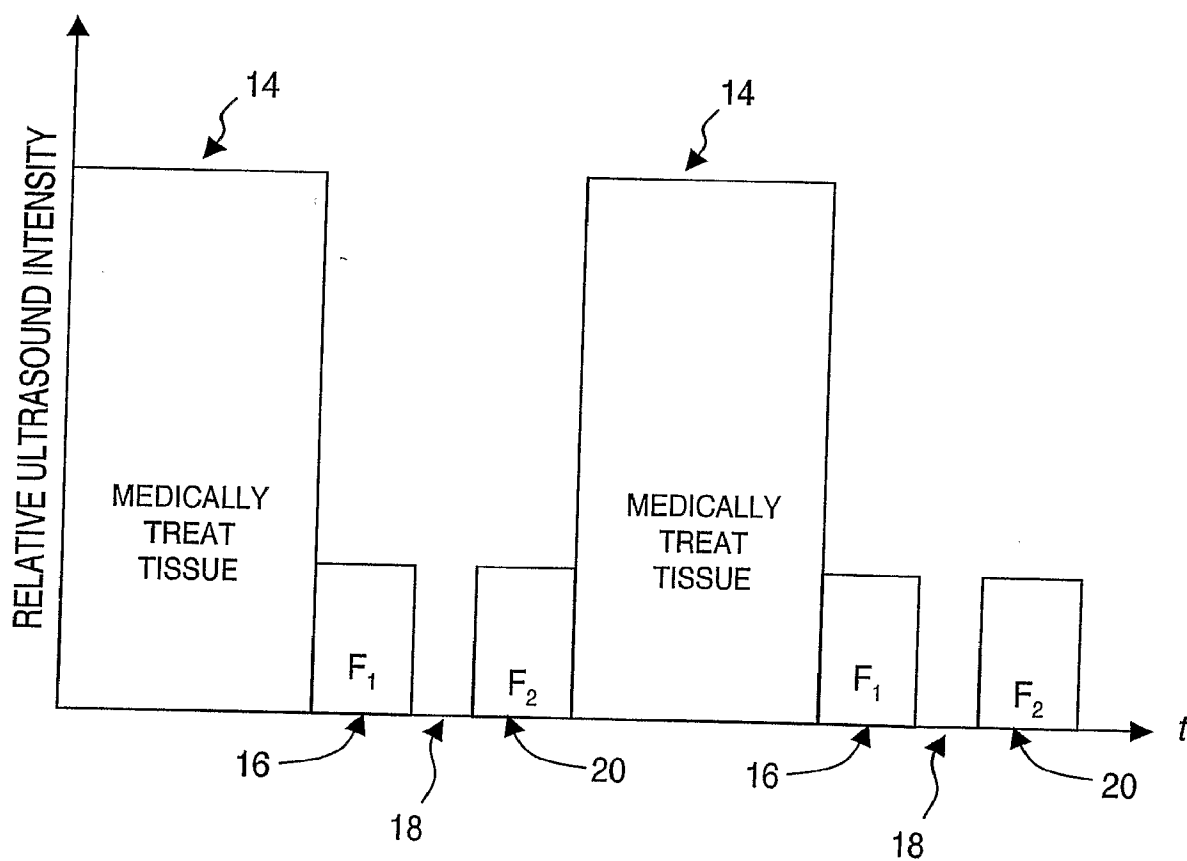


Fig. 2

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 3 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

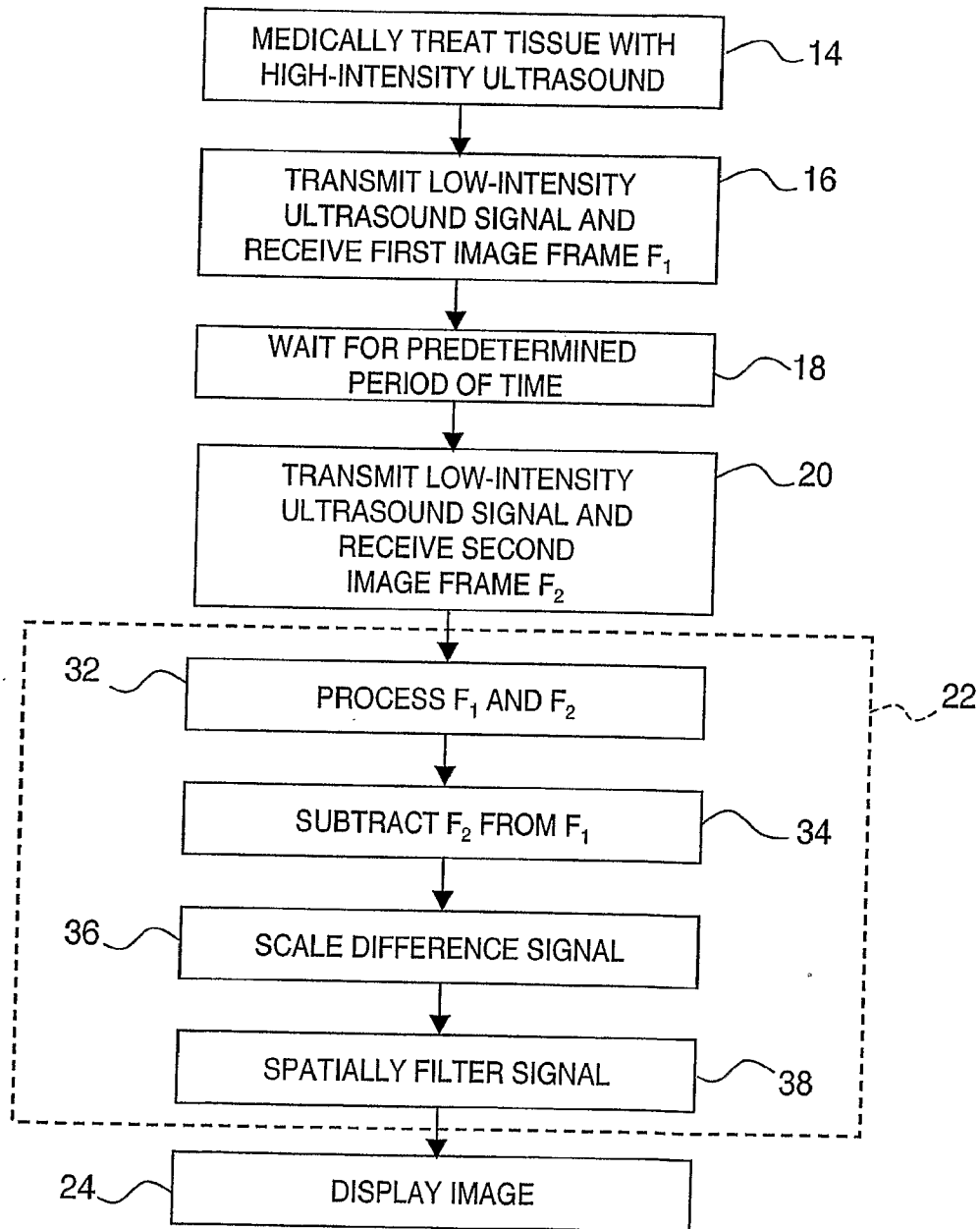
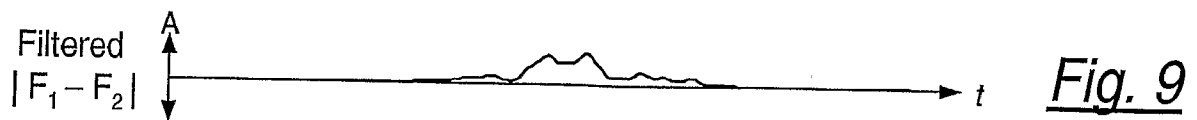
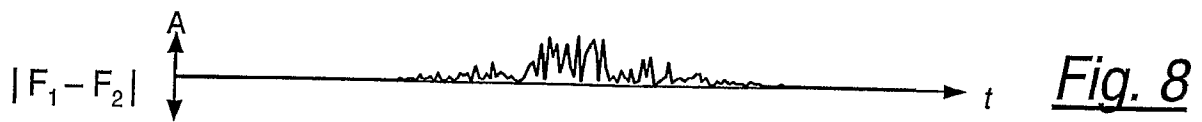
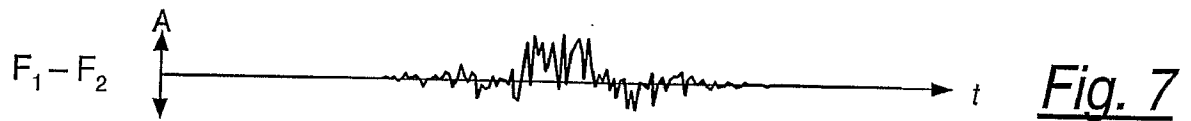
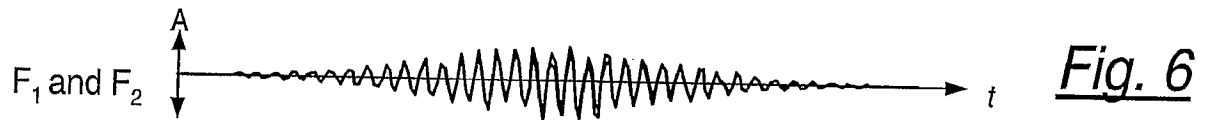
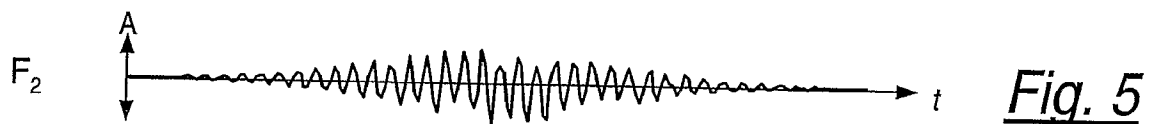
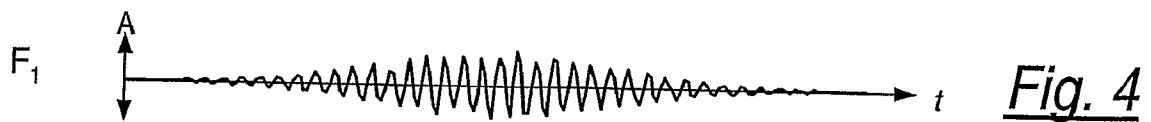


Fig. 3

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 4 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777



Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 5 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

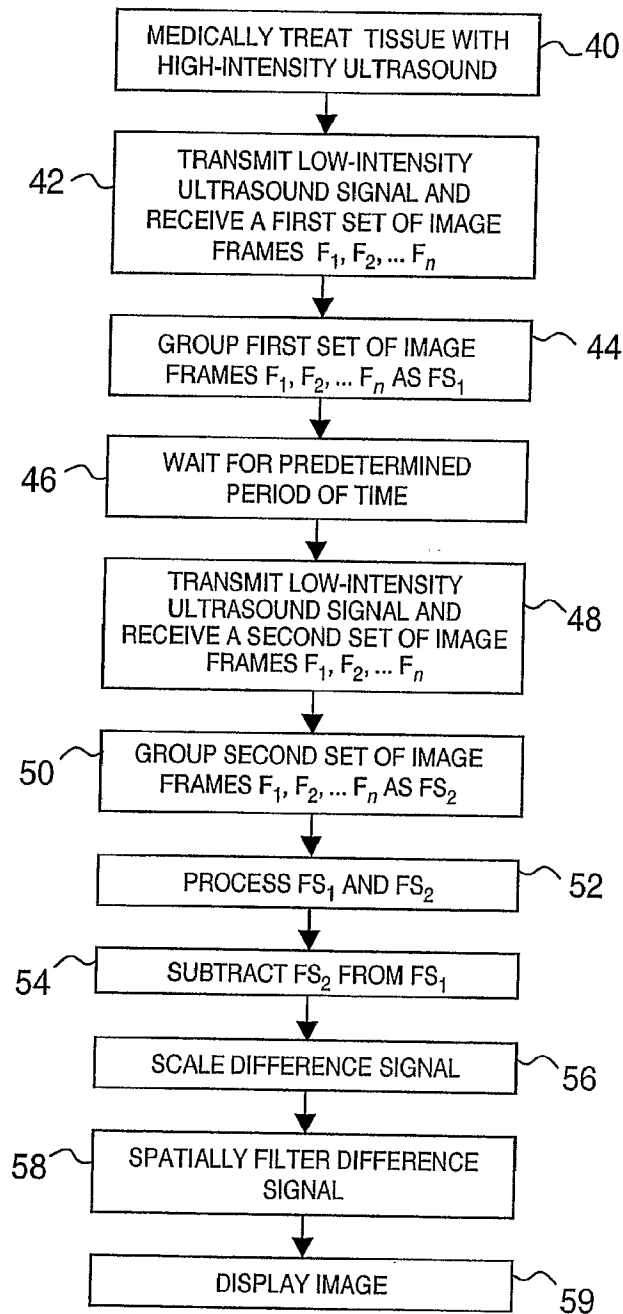


Fig. 10

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 6 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

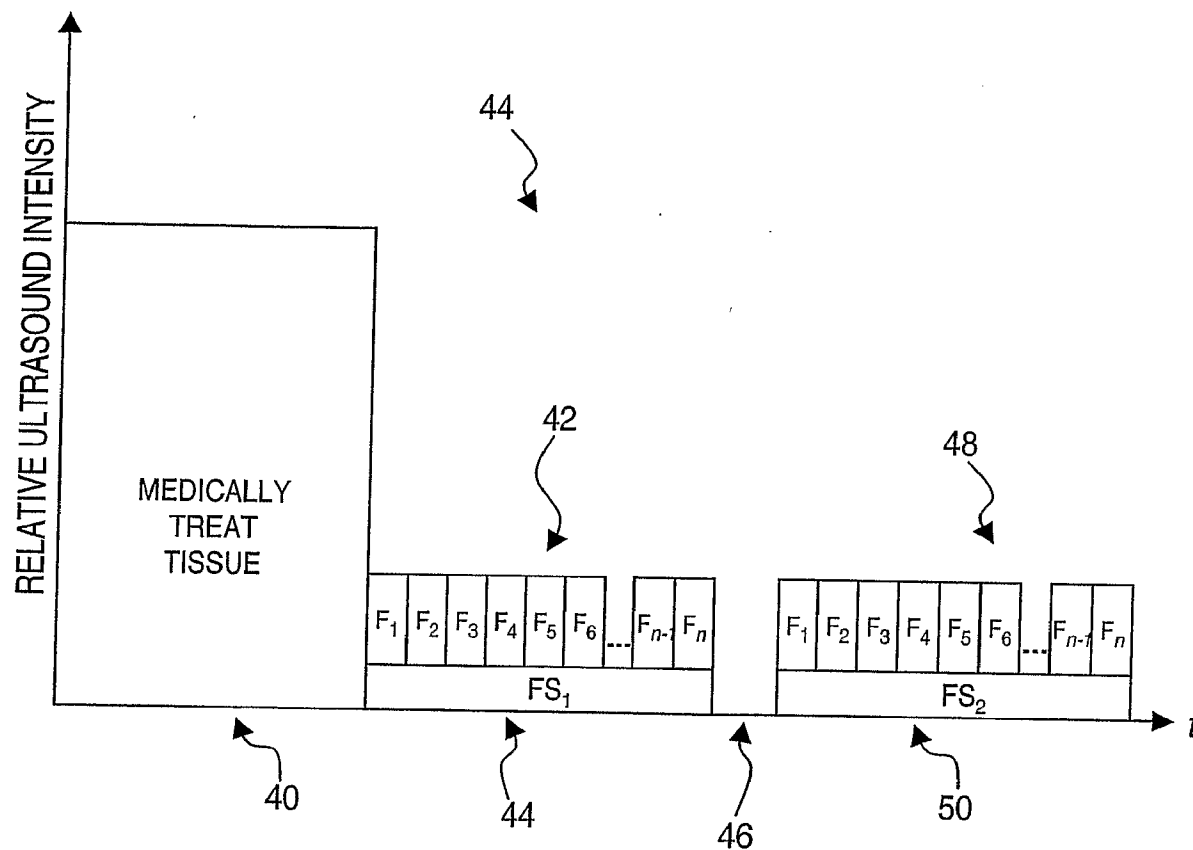


Fig. 11

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 7 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

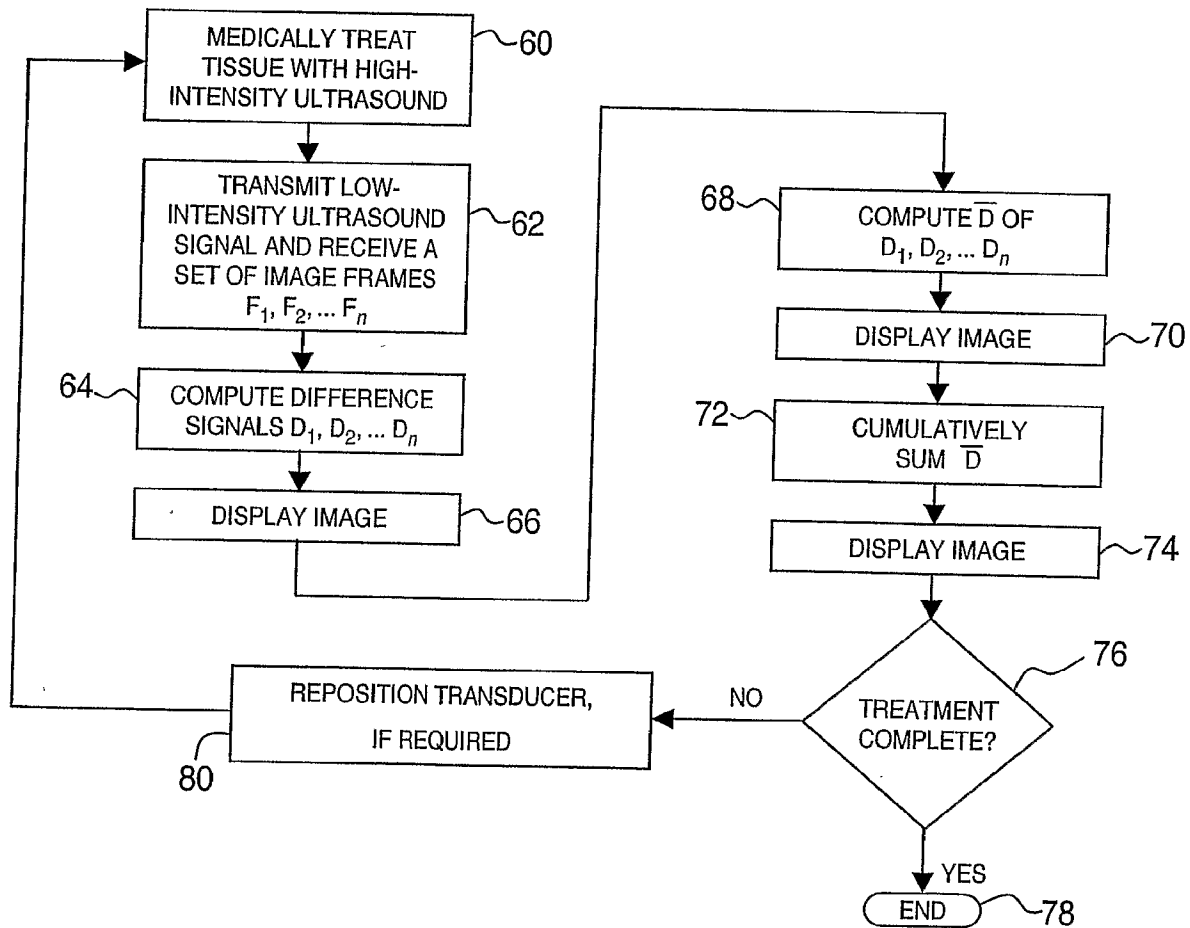


Fig. 12

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 8 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

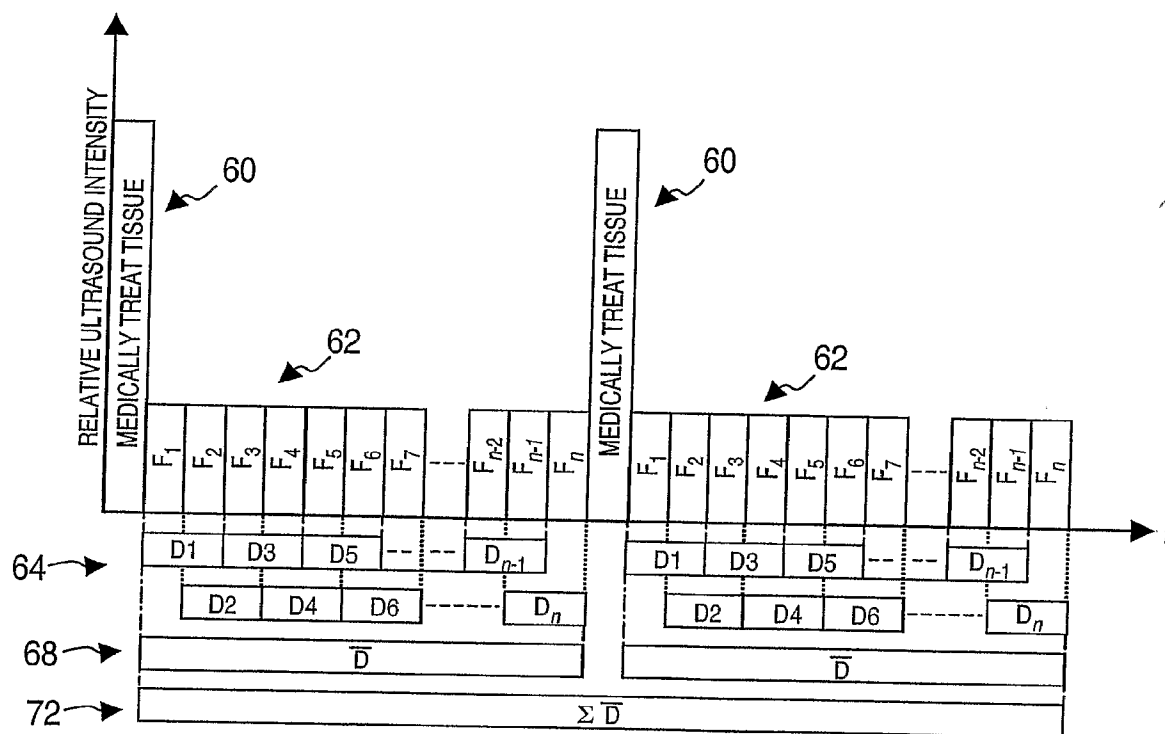


Fig. 13

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 9 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

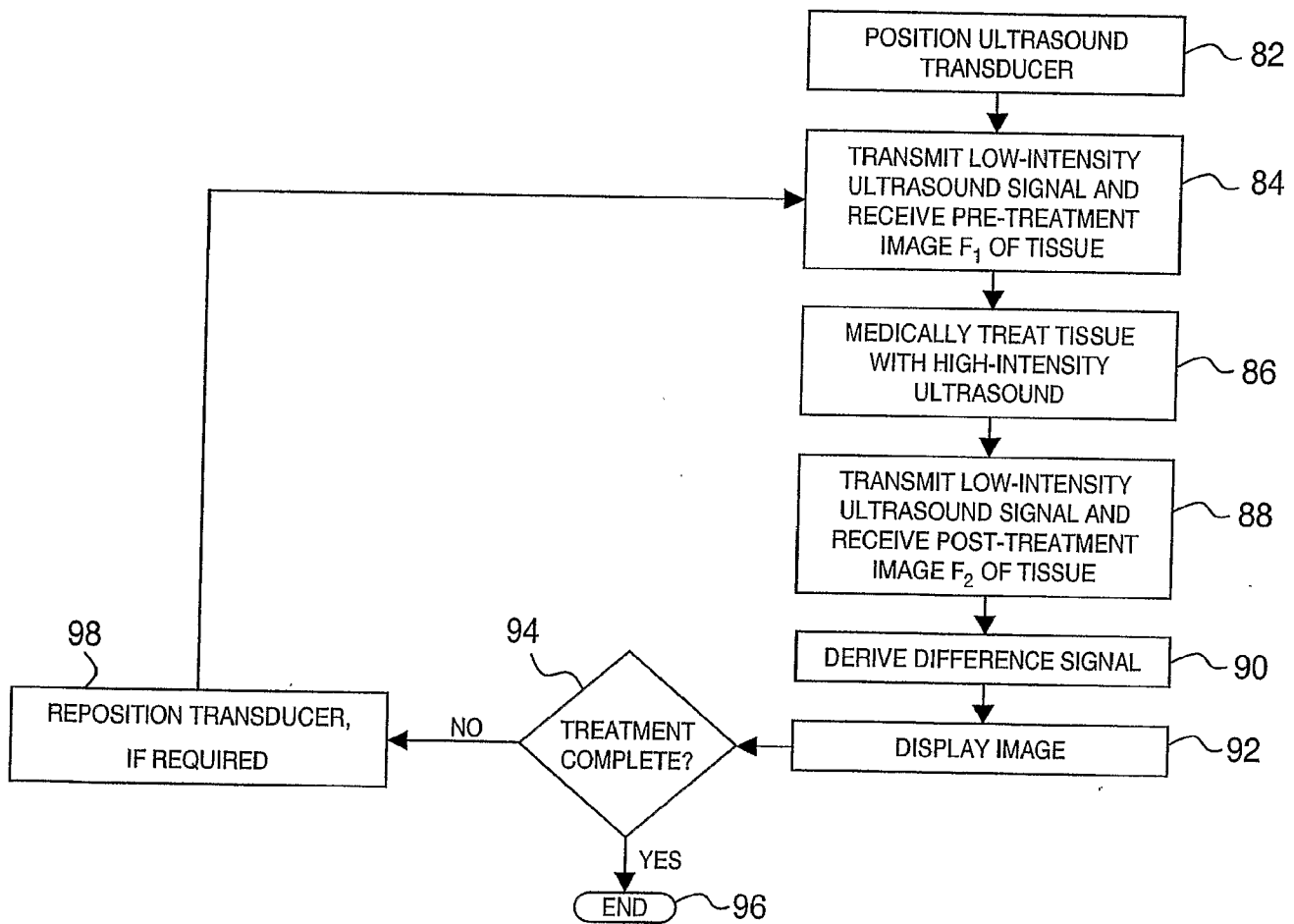


Fig. 14

Title: Method for Monitoring of Medical
Treatment Using Pulse Echo Ultrasound
Inventor: T. Douglas Mast
Sheet 10 of 10
Atty: Verne E. Kreger, Jr. Tel: 513-337-3295
Docket: END 5042
Cust. #000027777

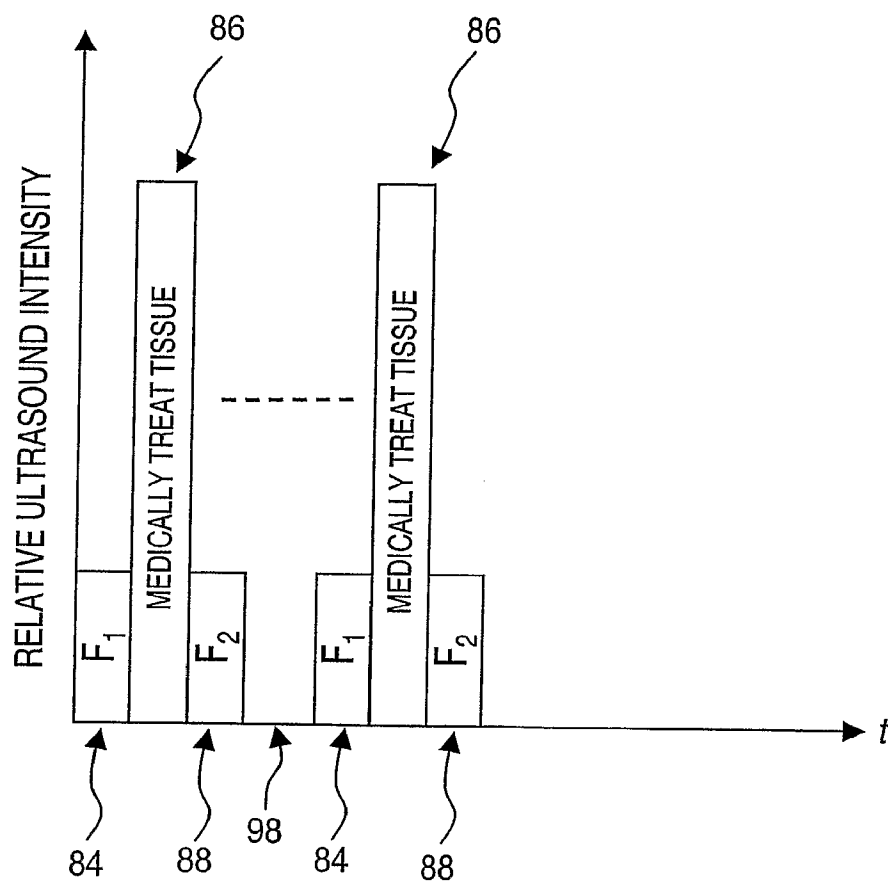


Fig. 15

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 December 2001 (27.12.2001)

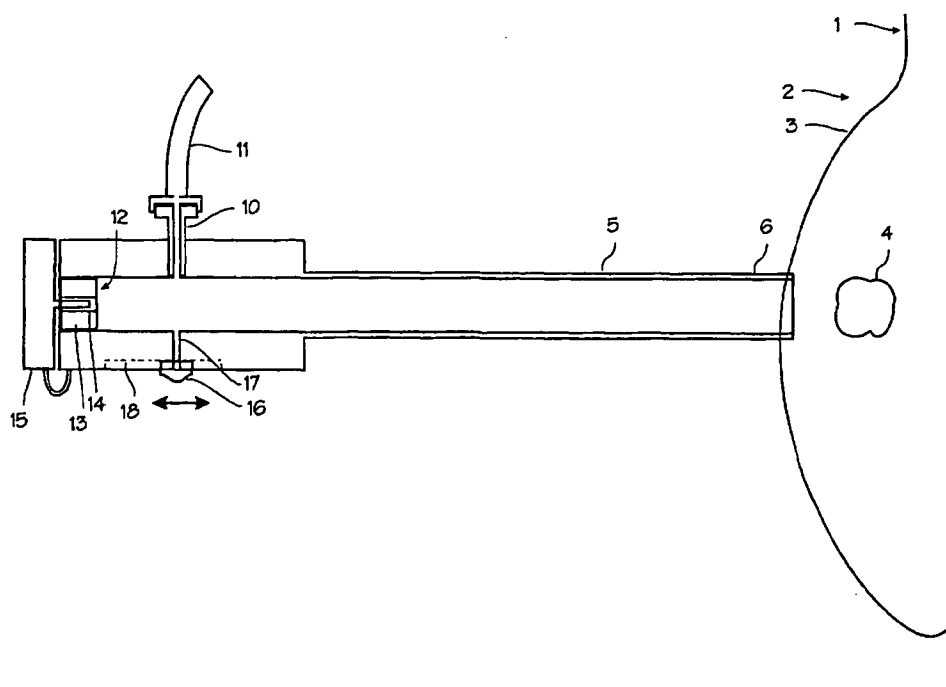
PCT

(10) International Publication Number
WO 01/97702 A1

- (51) International Patent Classification⁷: **A61B 18/18**
- (21) International Application Number: PCT/US01/19454
- (22) International Filing Date: 19 June 2001 (19.06.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
09/598,124 21 June 2000 (21.06.2000) US
- (71) Applicant: **SANARUS MEDICAL, INC.** [US/US]; 5673 W. Las Positas Blvd., Suite 218, Pleasanton, CA 94588 (US).
- (72) Inventors: **VAN BLADEL, Kevin, H.**; 5673 W. Las Positas Blvd., Suite 218, Pleasanton, CA 94588 (US). **STABINSKY, Seth**; 5673 W. Las Positas Blvd., Suite 218, Pleasanton, CA 94588 (US). **ZINDEL, Lisa**; 5673 W. Las Positas Blvd., Suite 218, Pleasanton, CA 94588 (US). **FOY,**
- (74) Agent: **CROCKETT, K., David**; Crockett & Crockett, 24012 Calle de la Plata, Suite 400, Laguna Hills, CA 92653 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: DEVICE FOR BIOPSY AND TREATMENT OF BREAST TUMORS



(57) Abstract: A device for diagnosis and treatment of tumors and lesions within the body. A cannula (5) adapted to apply suction through the lumen (22) of the catheter to the tumor or lesion is described. The lumen (22) has a self sealing valve (12) through which a cryoprobe (27) is inserted while the suction is being applied. The cryoprobe (27) is then inserted into the lesion, and operated to ablate the lesion.



WO 01/97702 A1

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Device for Biopsy and Treatment of Breast TumorsField of the Inventions

The devices and method described below relate to the diagnosis and treatment of breast lesions, and more generally, to the diagnosis and treatment of tumors and lesions throughout the body.

Background of the Inventions

Biopsy is an important procedure used for the diagnosis of patients with cancerous tumors, pre-malignant conditions, and other diseases and disorders. Typically, in the case of cancer, when the physician establishes by means of procedures such as palpation, mammography or x-ray, or ultrasound imaging that suspicious circumstances exist, a biopsy is performed. The biopsy will help determine whether the cells are cancerous, the type of cancer, and what treatment should be used to treat the cancer. Biopsy may be done by an open or percutaneous technique. Open biopsy, which is an invasive surgical procedure using a scalpel and involving direct vision of the target area, removes the entire mass (excisional biopsy) or a part of the mass (incisional biopsy). Percutaneous biopsy, on the other hand, is usually done with a needle-like instrument through a relatively small incision, blindly or with the aid of an imaging device, and may be either a fine needle aspiration (FNA) or a core biopsy. In FNA biopsy, individual cells or clusters of cells are obtained for cytologic examination and may be prepared such as in a Papanicolaou smear. In core biopsy, as the term suggests, a core or fragment of tissue is obtained for histologic examination which may be done via a frozen section or paraffin

section. One important area where biopsies are performed is the diagnosis of breast tumors.

Traditionally, the biopsy technique for breast tumors involves placing a biopsy device multiple times into the breast and taking several samples of tissue from a mass or tumor which is suspected of being cancerous. Several samples are required to be sure that some tissue from the suspect mass has been captured, and enough tissue has been sampled to ensure that, if disperse cancer cells exist in the suspect mass some of those cancer cells will be captured in the samples. Each time the device is placed the physician must locate and direct the device with ultrasound imaging into the correct position near the suspect mass. Some breast tumors and lesions are very well defined, hard spherical masses which grow within the soft, compliant breast tissue. It is difficult to force a needle into these lesions because they are resistant to puncture and fairly mobile. Forcing the biopsy needle into the lesion is like trying to spear an apple floating in water.

Vacuum assisted biopsy system proposed by Biopsys involves sucking a breast lesion into a cannula and shearing off the captured edge of the lesion to obtain a biopsy sample. The device uses a vacuum to collect tissue into the side of an open tubular device, and then uses a rotating corer to cut the tissue collected. The rotating core is slidable within the tubular section and can be pulled back to remove the tissue collected in the rotating core. An additional stylet inside the rotating core can be used to push the tissue out of the core. The device can be rotated on its axis to remove a sample, 360 degrees around the central placement of the device. Typically, physicians sample six to eight cores. One advantage of this device is that the physician does not have to remove the device for additional biopsy samples. However,

the tumor itself must be re-engaged after every coring operation, which entails substantial effort in relocation and confirmation that the target suspect mass has been engaged by the side aperture. Tumors may be too tough to yield to the suction and deform as necessary to enter the side opening of the cannula. Doctors also currently use the device to take a circular sequence of cores by rotating the device about its long axis or by sideways movement of the suction head to take a line of cores.

After biopsy and analysis, the tumor must be treated with a separate device, as Biopsys teaches that their coring device should not be used for resection. Indeed, the device is not designed to perform resection with assurance that complete resection of a suspect mass has been accomplished. Mechanical cutting and disruption of the tissue structure and cancer cell dispersion (that is, tearing of the tissue around the cancer and movement of the cancer cells amongst normal tissue) will result in unintentional delivery of cancer cells into healthy tissue adjacent the lesion.

Summary

The devices and methods described below provide for diagnosis and treatment of tumors within the breast. The devices include structures which permit the surgeon to secure a suspect mass or tumor within the breast for an extended period of time and for several biopsies, coring procedures, or resections. The suspect mass or tumor is secured to a cannula for the entire diagnostic and treatment procedure, or subsets of the procedure such as biopsy or ablation. This allows the placement of the cannula with a single step utilizing methods such as ultrasound to guide the cannula toward the tumor.

The cannula includes a lumen adapted to be connected to a source of vacuum, which can be used to secure a breast lesion

to the cannula. A ring seal on the proximal end of the catheter permits biopsy needles, cryoprobes or other ablation devices to be inserted through the cannula and into the lesion while the vacuum on the cannula is maintained. In this
5 manner, the needles and ablation devices may be inserted into the lesion while the lesion is held securely in place by the suction applied to the cannula.

Brief Description of The Drawings

Figure 1 illustrates the cannula adapted for use in
10 securing a breast tumor during a biopsy or ablation procedure.

Figure 2 illustrates the biopsy needle in use with the cannula of Figure 1.

Figure 3 illustrates a multiple coring needle which may be used with the cannula of Figure 1.

15 Figure 4 illustrates the placement of a cryoprobe or other ablative device within the cannula of Figure 1.

Figure 5 illustrates a method of breast tumor ablation for tumors located near the skin.

20 Figure 6 illustrates a method of breast tumor ablation for tumors located near the skin.

Figure 7 illustrates and adaptation of the cannula to provide additional protection to the skin.

Detailed Description of the Inventions

Figure 1 illustrates the biopsy and treatment device
25 adapted for use in securing a breast tumor during the biopsy and treatment procedure. The patient 1 and the patient's breast 2 and skin 3 of the breast are shown schematically. The tumor, lesion or other suspect mass 4 is located within

the breast, surrounded by soft tissue and fatty tissue. The tumor in this illustration is a well defined, hard mass ranging in size from 3 to 40 mm in diameter, typical of a benign palpable tumor or fibro-adenoma, although the device and method may be used to treat fibrocystic disease and other conditions. The device comprises a cannula 5 with a straight cut distal edge 6 adapted for insertion through a small incision in the skin overlying the tumor and a proximal end 7 which remains outside the breast. The proximal end of the cannula is fitted with hub 8 which serves as a handle and a manifold for the several connections to the cannula. This hub may be integral with the cannula or provided as a separate piece secured to the proximal end of the cannula. The cannula has a lumen 9 extending through the cannula from the distal edge to the proximal end of the cannula. On the hub, a vacuum connection 10 in the form of Luer fitting provides a fluid connection between the lumen of the cannula and a vacuum tube 11. The vacuum hose may be connected to any source of vacuum or suction. On the proximal end of the hub, a valve 12 seals the cannula proximal end against air pressure but allows passage of the needles and probes used in the procedure. The valve may be a self-sealing silicone plug 13 provided with a slit 14 capable of accommodating the needles and probes by resiliently expanding and conforming around a needle or probe when a needle or probe is forced through the slit, and resiliently closing to an airtight seal when the needles or probes are removed. Thus, the valve allows for insertion of various instruments and elongate medical devices while maintaining the seal necessary to provide sufficient suction to hold the tumor. A stopper or cap 15 is provided for insertion into the slit when the valve is not occupied by a needle or probe to positively seal the valve. A backup valve, such as ball valve which opens to form a clear and straight lumen, may be placed in line before the valve 12 in place of

the stopper. The cannula is made of an acceptable biological material such as Teflon, carbon fiber, metal or metal composite for maximum strength with minimal wall thickness. The self-sealing valve is comprised of silicone or other material of similar resilience and conformability. An additional valve 16 may be added on the proximal handle, controlling a port 17 communicating between the vacuum lumen and the exterior of the cannula. The valve illustrated is merely a thumbslide mounted in a recess 18. This valve may be used to break the vacuum established in the vacuum lumen to release a lesion from the distal tip of the device, or to bleed the vacuum from the lumen to lessen the suction on a lesion.

Figure 2 illustrates the cannula in use with a biopsy needle 20 in place within the lumen. A biopsy needle 20 fits within the lumen of the cannula and passes through the valve 12. The valve deforms and opens enough to allow the needle to pass through, yet still maintains a sufficiently airtight seal to maintain the vacuum within the cannula lumen. The needle has a sharp distal tip 21 which can pierce the tumor 4. The distal tip is shaped with a coring edge to collect tissue within the lumen 22 of the needle. As depicted in Figure 2, suction has been applied to the cannula lumen through the vacuum hose 11 and connection 10, thus drawing the tumor to the distal edge of the cannula and securely holding it in place. The biopsy needle has been inserted through the self-sealing valve and through the cannula lumen into and through the tumor. A small core of tumor tissue 23 has been forced into the lumen of the needle. The needle may now be removed and the core of tumor tissue extracted and analyzed for the presence of cancer cells. When the needle is removed, the suction is maintained on the cannula lumen and the tumor remains securely engaged with the cannula distal edge. The biopsy needle (or another) can then be inserted through the

cannula and into the tumor without having to relocate and reengage the tumor with the cannula. After all necessary biopsies have been taken, the sample tissue may be analyzed for the presence of cancer cells or other undesirable tissue
5 for which ablation is indicated.

Figure 3 illustrates a multiple coring needle 24 for use with the system. This needle includes several coring lumens 25 opening at the distal end of the needle into coring edges 26. The coring lumens are spaced in a circle about the
10 circumference of the needle, and extend from the distal tip 21 of the needle proximally to the proximal end of the needle. It may be used in place of the single biopsy coring needle as illustrated in Figure 2. By providing suction to one or more of the lumens, the tumor is secured to the coring needle.

15 Figure 4 illustrates the use of an ablative device, such as cryoprobe, with the cannula. The cryoprobe 27 fits within the lumen of the cannula and passes through the valve 12, and the distal tip of the cryoprobe is forced into the tumor until the active freezing portion of the probe resides within the
20 tumor. During placement of the cryoprobe, the vacuum is maintained within the lumen so that the tumor is securely engaged by the cannula. With the tumor secured by the vacuum, the cryoprobe may be easily forced into the tumor. The cryoprobe may be operated to ablate the tumor with cryogenic
25 freezing as required to destroy the tumor. To operate the cryoprobe, liquid or gas cryogenic fluids (such as liquid nitrogen, or gaseous argon in combination with a Joule-Thomson cryostat in the probe tip) are passed through the probe, supplied from a cryosurgical control system (not shown). The
30 operation of the cryoprobe creates an iceball 28 which encompasses the lesion 4, and cools the lesion to lethal cryogenic temperatures. Any ablation device may be used in place of the cryoprobe, including RF ablation probes,

microwave ablation probes, laser ablation probes, or focused ultrasound energy probes. Temperature sensors 29 may be mounted on the skin over the lesion in order to monitor skin temperature, so that the surgeon may avoid ablating the skin.

5 In use, the devices described above are used in place of traditional biopsy, coring and ablation devices. Prior to use, the patient is prepared and the breast is appropriately prepped and draped. The site is prepared using local anesthesia and, optionally, intravenous sedation. The patient
10 is positioned on an operating table in the supine position, with the patient on her back. (If the procedure is accomplished under stereotactic guidance, the patient may be prone on a stereotactic table, exposing the breast below the table.) The breast is imaged, if not previously imaged, to
15 determine the location of lesions. A small incision is made in the breast to allow the cannula to be easily inserted into the skin. The surgeon inserts the cannula into the patient's breast through the incision, pushes it into the breast until the distal edge of the cannula is proximate to the boundary of
20 the tumor. An ultrasound scanner, MRI, stereotactic, mammographic, infrared or other imaging device is used to obtain an image of the breast, including the tumor and any device inserted into the breast, and the surgeon uses the display from the imaging device to assist in guidance of the
25 cannula to the tumor. With the cannula distal edge in position near the tumor, the surgeon applies vacuum to the cannula through the side port on the cannula. The vacuum draws the tumor toward the cannula, and the cannula securely engages the tumor until the suction is broken at the end of
30 the procedure. The surgical biopsy needle can be inserted through the cannula and into the tumor to retrieve a sample of tissue for analysis. Because coring can be accomplished without removing the portion of the tumor engaged by the cannula, or otherwise disrupting the suction between the

cannula and the tumor, several biopsy samples may be taken without having to relocate and re-engage the tumor.

Depending on the analysis of the biopsy (whether or not the samples obtained contain cancerous cells or other conditions), treatment of the tumor may be required. If analysis can be accomplished intra-operatively (that is, during a period of time in which it is feasible to keep the patient in the operating room and maintain the tumor engaged with the cannula), and indicates the presence of cancerous cells or other condition for which ablation is indicated, an ablation instrument can be inserted through the cannula and into the tumor. If so, the surgeon inserts an ablation instrument, such as a small caliber cryoprobe, into the tumor. Preferably, the surgeon inserts a cryoprobe through the valve and cannula and into the tumor, while maintaining suction on the cannula. The surgeon initiates cooling of the cryoprobe, and cools the tumor through one or more cycles of cooling to cryogenic temperatures and subsequent warming and thawing. A double freeze-thaw cycle is currently recommended. Each cycle consists of a 6 to 15 minute freeze followed by thawing until the internal cryoprobe temperature reaches 0°C (approximately 6 to 15 minutes). The device may also be used without regard to biopsy results. Patients prefer to have these lesions treated, even if they prove to be benign. In current practice, should biopsy results indicate the presence of cancer, the patient must return to the operating room shortly after the biopsy, undergo preparation, anesthesia, relocation of the lesion and ablation. Instead, the lesions may be ablated intraoperatively with the biopsy, immediately after biopsy and without interrupting the procedure to await the biopsy results. Should the biopsy prove negative for the presence of cancer, the patient will have received a substantially cosmetic treatment. Should the biopsy prove positive, the patient will have received a necessary

therapeutic procedure. In addition to the ablative procedure, the positive biopsy may indicate the need for additional monitoring and treatment.

For lesions deeper than 1 cm from the skin surface, the cryoprobe is advanced until the distal tip is located approximately in the center of the lesion or just beyond the lesion. For smaller lesions (<2cm diameter) the ice ball may grow beyond the margins of the tumor, while for larger lesions, the ice ball may remain within the confines of the tumor. The cryoprobe tip temperatures and skin mounted thermocouple readings are monitored throughout the ablation procedure. If the temperature of the skin overlying the cryoprobe measures below freezing, freezing operation of the cryoprobes should be paused until it returns to 10°C (the temperature at the edge of the ice ball edge is 0°C and exposure to such a temperature for the few minutes will not harm the skin, but caution should always be employed).

The procedure may be augmented with additional steps. Just prior to ablation treatment, prophylactic antibiotics can be administered at the surgeon's discretion. Just prior to cryosurgical ablation, cryogenic enhancement agents may be injected directed into the tumor through a hypodermic needle inserted through the valve and cannula and into the tumor while it is secured by suction to the cannula. During cooling operation of the cryoprobes, warm saline may be washed over the skin overlying the tumor and iceball to prevent freezing of the skin.

If the lesion being treated is close to the skin such that cryoablation of the lesion entails a danger of cryoablation of the overlying skin, several milliliters of a resorbable material such as sterile saline may be injected or inserted into the subcutaneous tissue between the skin and the

lesion. This will create a thermally protective mass or barrier layer between the tumor and the skin. Thermal protection may arise from insulative effect of the thermally protective mass or merely by the distension or separation of the skin away from the tumor and thus away from the iceball. As illustrated in Figure 5, where the tumor 4 is close to the skin 3, the thermally protective mass 30 is injected between the skin 3 and the subcutaneous fat 31 of the breast. When the cryoprobe 27 is operated to create the iceball, the iceball 32 either grows into the thermally protective mass or is inhibited in growth in the direction of the thermally protective mass (as illustrated by the non-spherical shape of the iceball in this illustration). This method basically distends the skin away from the iceball. This may also be accomplished by dissecting the skin away from the tumor with a balloon inserted between the skin and fat in the area overlying the tumor. Balloon dissection can be accomplished as illustrated in Figure 6. Here, a balloon 33 has been inserted subcutaneously between the tumor 4 and the overlying skin 3. The balloon is inflated with air or other sterile gas, through inflation tube 34, creating a good layer of insulation between the cryoprobe and the overlying skin.

Figure 7 illustrates and adaptation of the cannula to provide additional protection to the skin. The cryoprobe 27 is inserted through a side lumen 35 provided on the cannula 5. The breast lesion 4 is drawn by vacuum to the tip of the cannula. The cryoprobe is advanced distally out of the side lumen until the freezing region underlies the lesion, and it is operated to create the iceball 36. The iceball extends superficially toward the skin and to encompass the lesion, and also extends posteriorly into the breast, where some healthy breast tissue is ablated but the overlying skin is not. This system and procedure also has the advantage that the lesion itself is not punctured, limiting the potential for seeding

due to the release of cancerous cells from the disruption of the tissue of the tumor.

The cannula illustrated above is preferably 10 to 20 cm in length and about 3 mm in diameter with an internal diameter of 2.8 mm, and a clearance of about .25 mm between the inner bore of the cannula and any device inserted through the cannula during suction. The cryoprobes may be Joule-Thomson probes, liquid cryogen probes, or probes of other designs. Various other ablative devices may be used in place of the cryoprobe, including laser ablation devices, RF ablation devices, chemical ablation catheters and any other ablative technology proposed for use to destroy tumors and lesions. The vacuum applied is preferably in the range of 14 to 21 inches of mercury vacuum.

The devices and methods illustrated above have been illustrated in relation to the treatment of tumors and lesions within the breast. However, they may be used to treat tumors and lesions throughout the body wherever the tumors which are difficult to secure and locate are encountered, and wherever nearby tissue must be protected from freezing. Thus the devices and methods may be used for tumors and lesions of the uterine tube (such as uterine fibroids), kidney, liver, prostate or brain.

Thus, while the preferred embodiments of the devices and methods have been described in reference to the environment in which they were developed, they are merely illustrative of the principles of the inventions. Other embodiments and configurations may be devised without departing from the spirit of the inventions and the scope of the appended claims.

We claim:

1. A device for performing a biopsy of a mass within the breast of a human patient, said device comprising:

5 a cannula adapted for insertion into the body of the patient, said cannula having a distal end and a proximal end, and a lumen extending through the cannula and defining a proximal opening and a distal opening in the cannula;

10 a fitting disposed on the proximal end of the cannula, said fitting adapted for connection to a vacuum source;

an airtight seal in the proximal opening of the cannula, said airtight seal permitting passage of needles and cryoprobes through the seal while substantially maintaining the airtight seal.

15 2. A system for treating or sampling of a mass within the breast of a human patient, said system comprising:

20 a cannula adapted for insertion into the body of the patient, said cannula having a distal end and a proximal end, and a lumen extending through the cannula and defining a proximal opening and a distal opening in the cannula;

a fitting disposed on the proximal end of the cannula, said fitting adapted for connection to a vacuum source;

25 an airtight seal in the proximal opening of the cannula, said airtight seal permitting passage of elongate medical devices through the seal while substantially maintaining the airtight seal;

a source of vacuum pressure operably connected to the fitting;

an elongate medical device capable of insertion through the airtight seal and into the cannula, said elongate medical device being long enough to extend from the proximal end of the cannula to a distance outside the distal opening of the cannula.

3. The system of claim 2 wherein the elongate medical device is a biopsy needle.

4. The system of claim 2 wherein the elongate medical device is a cryoprobe.

5. The system of claim 2 wherein the elongate medical device is an ablation device suitable for ablation of the mass.

6. A method of performing cryosurgery of a lesion in the body of a patient, said method comprising;

inserting a cannula into the body of the patient so that the distal edge of the cannula is proximate the lesion;

applying suction to a lumen of the cannula, thereby drawing the lesion toward the cannula;

inserting an ablative medical device through the lumen of the cannula and into the lesion;

operating the ablative medical device to ablate the lesion.

7. A method of performing cryosurgery of a lesion in the body of a patient, said method comprising;

inserting a cannula into the body of the patient so that the distal edge of the cannula is proximate the lesion;

applying suction to a lumen of the cannula, thereby
drawing the lesion toward the cannula;

inserting a cryoprobe through the lumen of the cannula
and into the vicinity of the lesion;

5 operating the cryoprobe to ablate the lesion.

8. A method of performing cryosurgery of a lesion in the
breast of a patient, the lesion being located under a portion
of overlying skin, said method comprising;

10 providing a cannula, said cannula having a distal tip and
a lumen adapted for application suction to the distal
tip thereof, and inserting the cannula into the body of
the patient so that the distal tip of the cannula is
proximate the lesion;

15 applying suction to a lumen of the cannula, thereby
drawing the lesion toward the distal tip cannula;

inserting a cryoprobe into the breast and into the
vicinity of the lesion;

operating the cryoprobe to ablate the lesion.

9. The method of claim 8 further comprising:

20 inserting the cryoprobe into the lesion by inserting it
through the lumen of the cannula and then advancing the
cryoprobe distally from the lumen of the cannula and
into the lesion.

10. The method of claim 8 further comprising:

25 inserting the cryoprobe into the lesion.

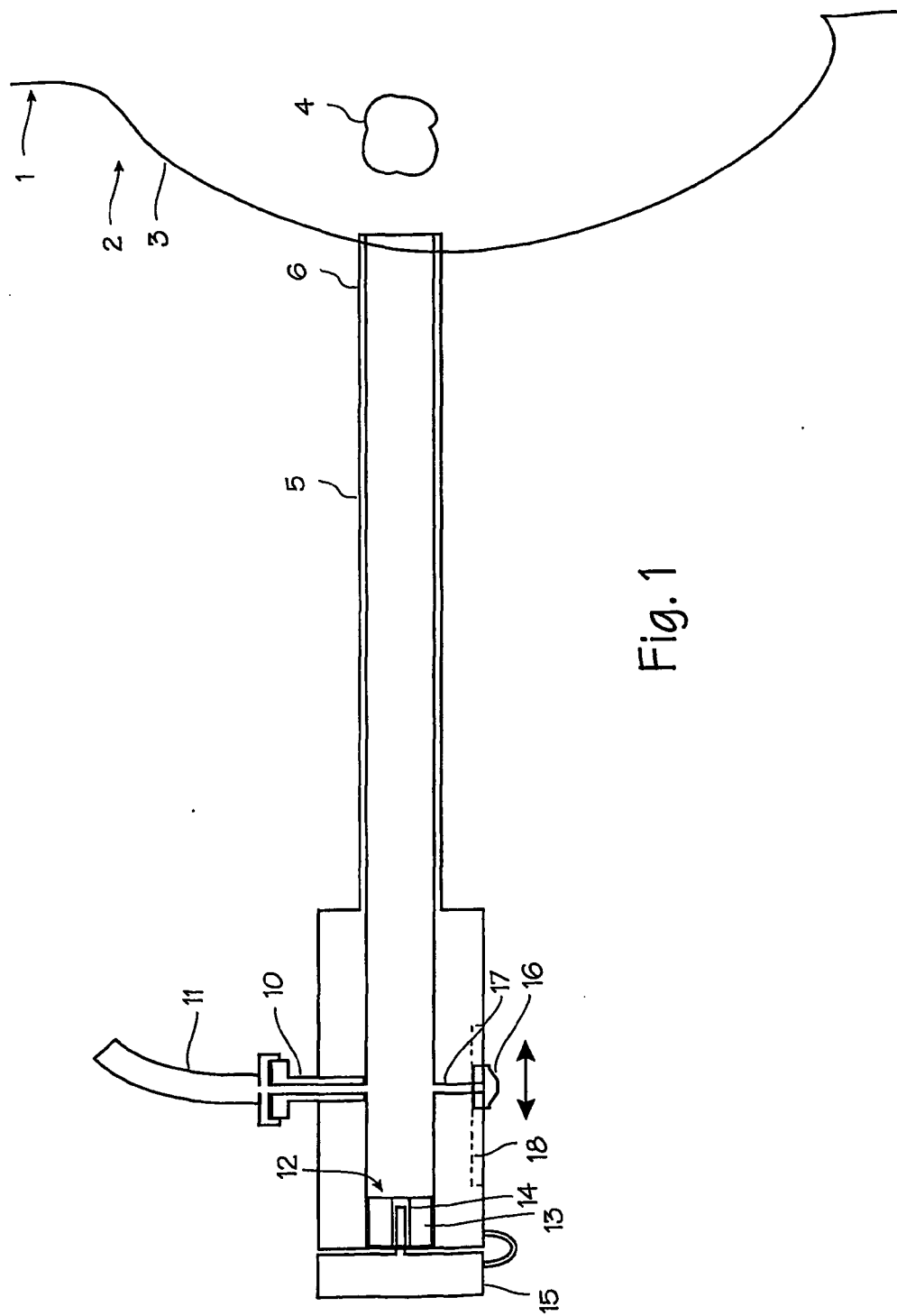
11. The method of claim 8 further comprising:

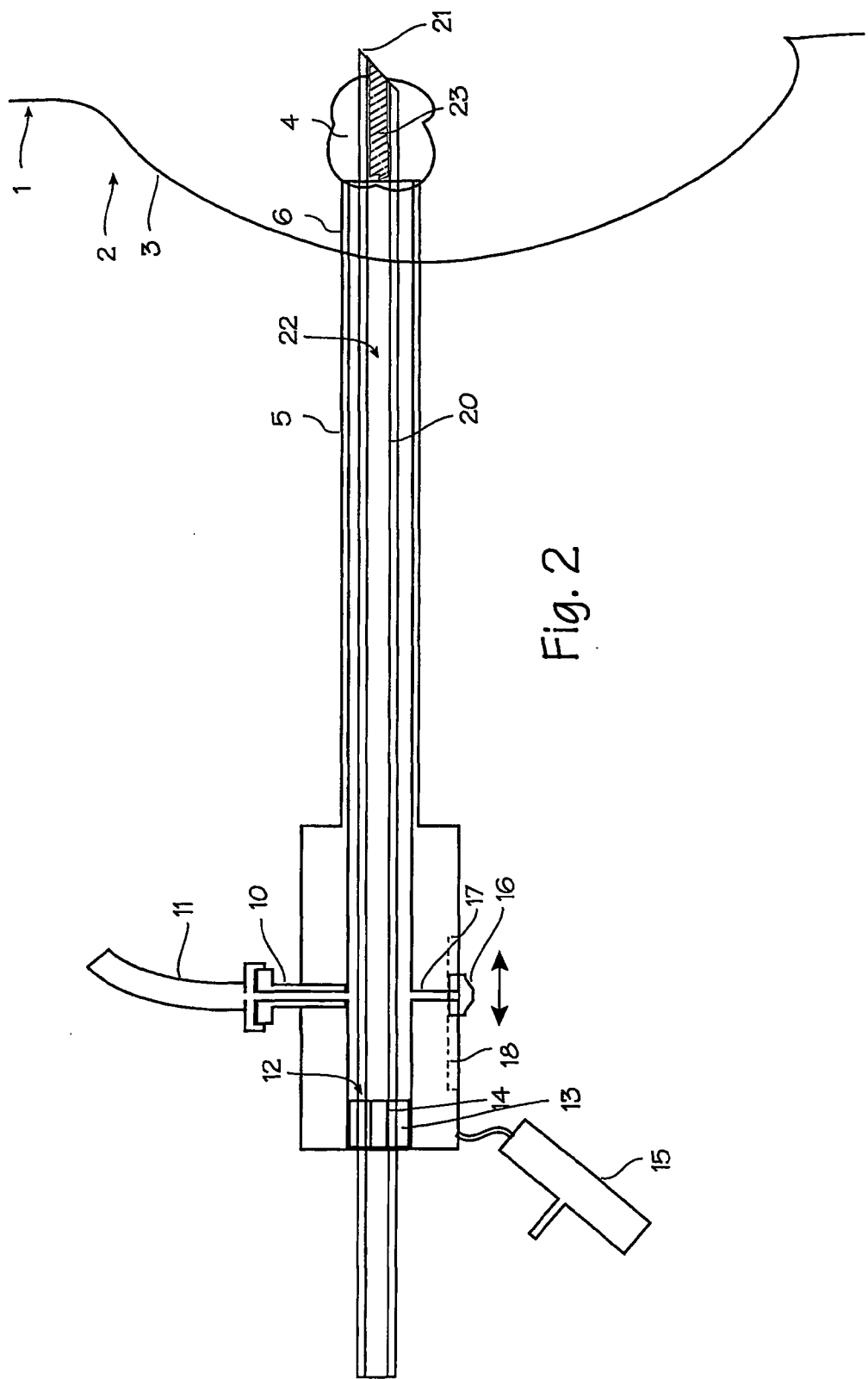
inserting the cryoprobe into the breast in a position
posterior to the lesion.

12. The method of claim 8 further comprising:

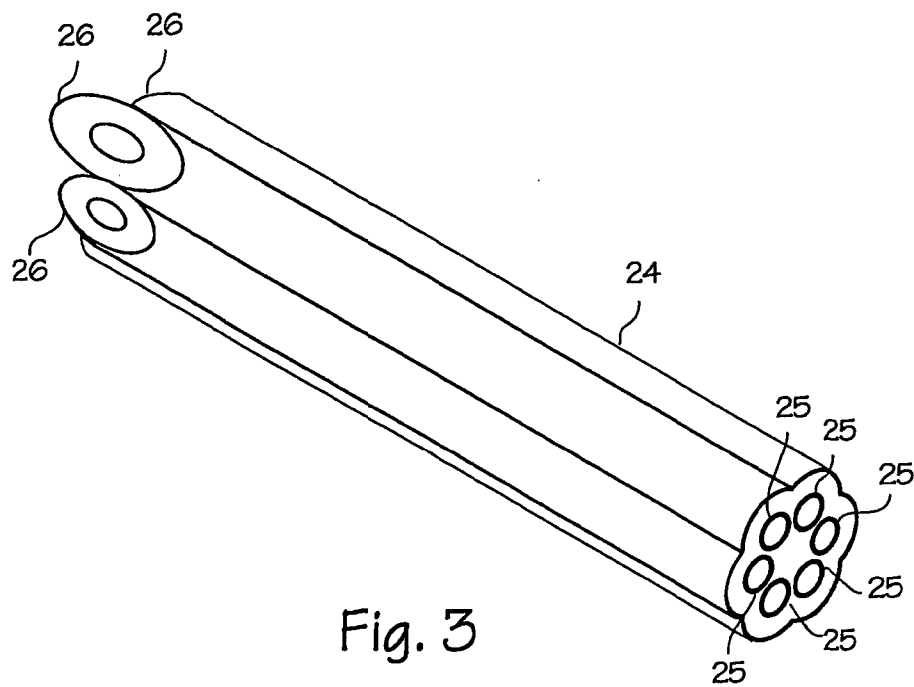
5 placing a thermally protective mass between the lesion
 and the overlying skin prior to operating the cryoprobe
 to ablate the lesion.

1/5

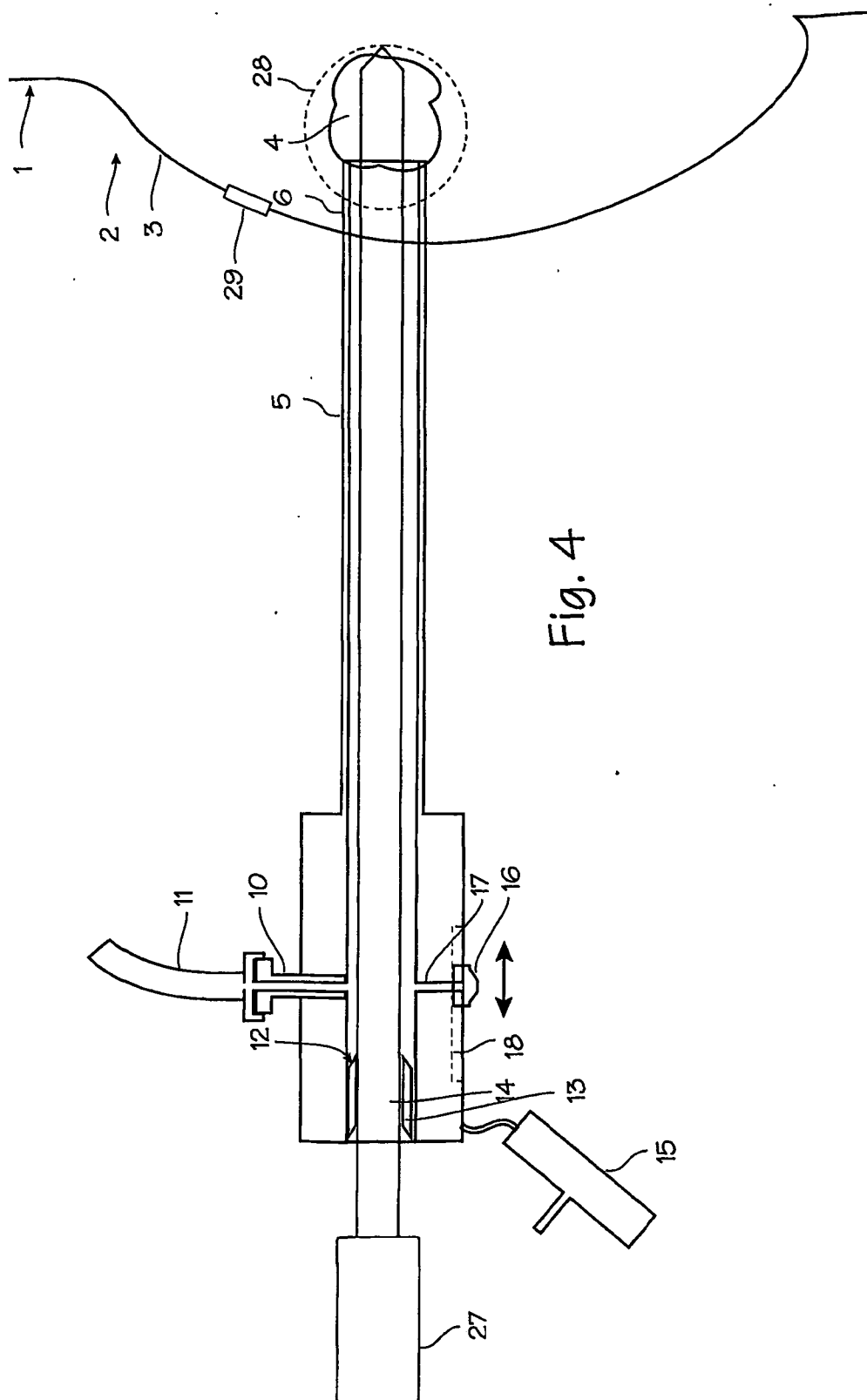




3/5



4/5



5/5

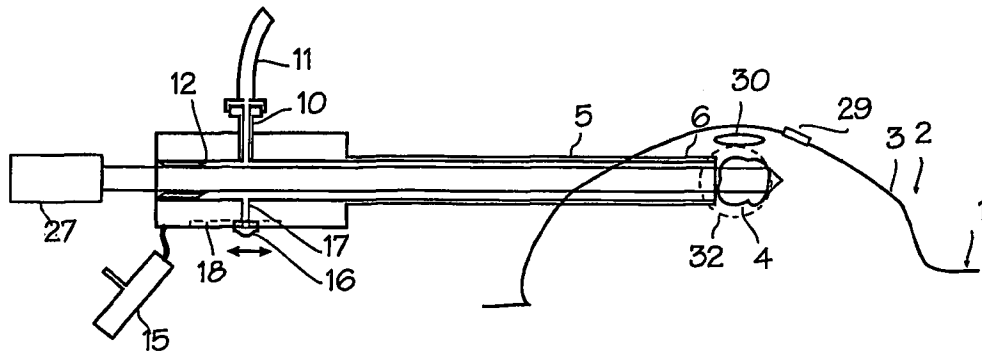


Fig. 5

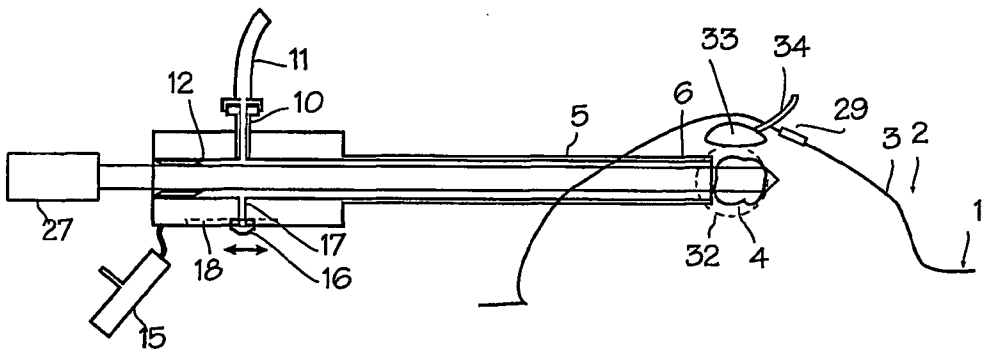


Fig. 6

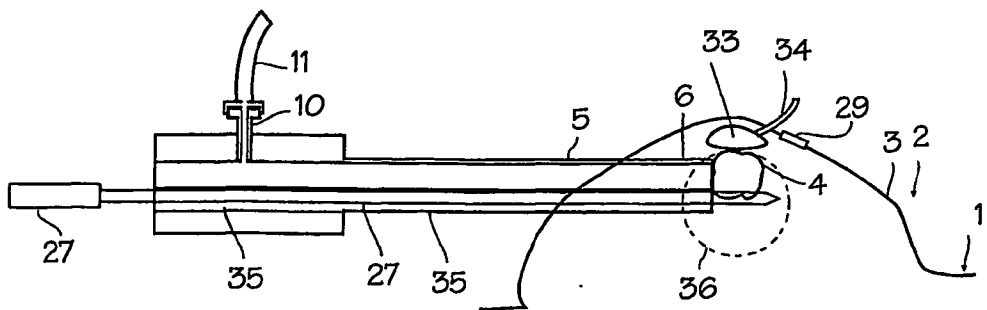


Fig. 7

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/19454

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61B 18/18

US CL :606/90

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/1, 90-26; 600/565-567

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,713,368 A (Leigh) 03 February 1998, whole document.	1-3
—		---
Y		4-7
Y	US 6,032,675 A (Rubinsky) 07 March 2000, whole document, figure 2.	4-7

☐ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

05 SEPTEMBER 2001

Date of mailing of the international search report

06 NOV 2001

 Name and mailing address of the ISA/US
 Commissioner of Patents and Trademarks
 Box PCT
 Washington, D.C. 20231

Facsimile No. (703) 305-8230

Authorized officer

MICHAEL PEFFLEY

Diane Smith f

Telephone No. (703) 308-0858

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record.**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☒ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.